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| (54) Title: <b>METHOD OF TREATING EYE DISORDERS WITH SILICONE/FLUROSILICONE COPOLYMER OIL</b><br>(57) Abstract<br><p>A method of treating an intraocular structural disorder of an eye comprising introducing into the intraocular structure under treatment a liquid silicone/fluorosilicone oil in an amount effective to treat the intraocular structural disorder.</p>   |  |  |

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METHOD OF TREATING EYE DISORDERS WITH  
SILICONE/FLUOROSILICONE COPOLYMER OIL

RELATED APPLICATION

This application is a continuation in part of copending application serial number 08/027,253, filed on March 5, 1993.

GOVERNMENT RIGHTS

This invention was made under NIH Grant RO1EY00327. The government has certain rights in this invention.

FIELD OF INVENTION

This invention relates to methods of treating eye disorders with a liquid silicone/fluorosilicone copolymer oil that has a relatively low tendency toward intraocular emulsification, and a specific gravity just greater than water so that it is effective to push back and maintain in place an inferior detached retina.

BACKGROUND OF INVENTION

There have been proposed and used a number of gases and liquids for treating eye disorders. Liquids that have been used as intraocular tools include silicone oils (polydimethylsiloxanes), fluorosilicone oils such as polymethyl-3,3,3-trifluoropropylsiloxane and a number of perfluorocarbon liquids, for example perfluorooctane, perfluorodecalin and perfluorophenanthrene (perfluorotetradecahydrophenanthrene).

One use of these liquids is in vitreoretinal surgery. The properties of the liquid for such use should be that it is transparent with a refractive index close to that of the vitreous. The substance should not mix with the vitreous, nor should it disperse or emulsify in the vitreous. Of course it should also be chemically and physiologically inert. To effectively act as a retinal tamponade, the substance should have a high interfacial tension and a high surface tension.

Silicone oils have been used for a number of years in vitreoretinal surgery. They are also known to be used for treating other disorders of the eye as set forth in U.S.

1 Patent Number 4,490,351, incorporated herein by reference. Silicone oil is transparent  
2 with a refractive index of 1.404 (the refractive index of water is 1.33), and a specific  
3 gravity of 0.97. It has a relatively high interfacial and surface tension, making it useful  
4 as a retinal tamponade. However, because the specific gravity of silicone oil is less than  
5 that of water, it is not useful as a tamponade for an inferior detached retina. Further, the  
6 viscosity of the silicone oils commonly used in vitreoretinal surgery is from 1,000 to  
7 12,000 cs. The high viscosity makes it relatively difficult to handle, requiring the  
8 surgeon to use a silicone oil pump to pump the liquid through the needle in to and out  
9 of the eye.

10 Fluorosilicone oil has a higher specific gravity of 1.29 and also has a relatively  
11 high surface and interfacial tension. The fluorosilicone oils in experimental use have a  
12 viscosity in the same range as the silicone oil. Accordingly, they are just as difficult to  
13 work with. An additional problem with the silicone oils and the fluorosilicone oils,  
14 however, is their tendency to emulsify in the eye. It is theorized that the dispersion of  
15 the fluorinated oil is stabilized in the eye by surface active proteins that interact with the  
16 highly electronegative fluorine atoms pendant on the polysiloxane backbone.  
17 Accordingly, fluorosilicone oils do not appear to be useful as long-term vitreous  
18 replacements for vitreoretinal surgery.

19 A number of perfluorocarbon liquids have also been investigated for treating eye  
20 disorders, particularly for intravitreal surgery. The relatively high specific gravity of  
21 about 2 makes them useful as a tamponade for an inferior detached retina. The high  
22 density could, however, damage the sensitive retinal tissue. In addition, the viscosity of  
23 the fluorocarbon liquids is only from about 1 to 8 cs, leading to more potential for  
24 emulsification in the vitreous. Further, the extremely high specific gravity also increases  
25 the chances of dispersion of the liquid in the vitreous. This dispersion, or "fish egging",  
26 of the perfluorocarbon liquids is more pronounced because of the number of fluorine  
27 atoms present in the compound that act to stabilize the dispersed liquid droplets.  
28 Accordingly, these liquids must be replaced in a second surgical procedure soon after the  
29 first repair procedure.

30 The use of silicone oil and perfluorocarbon liquids together has also been studied.  
31 See, for example, Ophthalmic Surgery "Long-Term Vitreous Replacement in Primates  
32 with Intravitreal Vitreon or Vitreon Plus Silicone", G.A. Peyman et al., V. 22, No. 11,

1 November 1991, pages 657-664; Retina "Experimental Studies of the Combined Use of  
2 Vitreous Substitutes of High and Low Specific Gravity", J.R. Sparrow et al., V. 12, No.  
3 2, 1992, pages 134-140. The silicone oil is useful as a tamponade for superior retinal  
4 detachments, and the perfluorocarbon for inferior retinal detachments. If the two could  
5 be used together, they would provide tamponade and mechanical support of both portions  
6 of the retina simultaneously. However, since the liquids are immiscible, the volumes of  
7 each would have to be carefully controlled for effective use. In addition, the great  
8 viscosity and density differences between the liquids would lead to a greater tendency  
9 toward dispersion, which would be offset to some extent by the lower fluorine  
10 concentration as compared to pure perfluorocarbon liquid (but not as compared to pure  
11 silicone oil). Because perfluorocarbons are used, however, such a procedure would  
12 require that the tamponade be relatively quickly removed and replaced in a second  
13 surgical procedure.

#### 14 15 SUMMARY OF INVENTION

16 It is therefore an object of this invention to provide a substance that is well suited  
17 for treating various eye disorders.

18 It is a further object of this invention to provide methods of treating eye disorders  
19 with a liquid silicone/fluorosilicone copolymer oil.

20 It is a further object of this invention to provide a vitreoretinal surgery method  
21 employing a substance that has a specific gravity just greater than the vitreous so that it  
22 may be used to push back and maintain in place an inferior detached retina without  
23 damaging the retina.

24 It is a further object of this invention to provide such a method employing an oil  
25 that can be used to manipulate the retina and can be left in the eye for sufficient time to  
26 allow healing of the retina before removal.

27 It is a further object of this invention to provide such a method employing an oil  
28 of relatively low viscosity.

29 It is a further object of this invention to provide such a method employing an oil  
30 with a relatively low tendency to emulsify in the vitreous.

31 It is a further object of this invention to provide such a method employing an oil  
32 which has a lower tendency to disperse in the vitreous.

1 It is a further object of this invention to provide such a method employing an oil  
2 which has less fluorine than fluorosilicone oils and perfluorocarbon liquids.

3 It is a further object of this invention to provide such a method employing an oil  
4 that is relatively easy for the surgeon to inject and remove from the eye.

5 It is a further object of this invention to provide such an oil that can act on both  
6 the anterior and posterior retina at the same time.

7 It is a further object of this invention to provide such an oil that can do away with  
8 the first removal procedure required with other compounds.

9 It is a further object of this invention to provide such an oil that can also deliver  
10 a drug such as an anti-proliferative agent.

11 This invention results from the realization that eye disorders, particularly detached  
12 and/or torn retinas, can be effectively treated employing a silicone/fluorosilicone  
13 copolymer oil that is just heavier than water, has a refractive index close to that of the  
14 vitreous, has a relatively low viscosity, and a relatively high surface tension and  
15 interfacial tension so that it is an effective tamponade for an inferior detached retina.

16 This invention features methods of treating intraocular structural disorders of an  
17 eye. In one embodiment the method includes introducing into the intraocular structure  
18 under treatment a liquid copolymer of silicone oil and fluorosilicone oil (silicone/  
19 fluorosilicone copolymer oil) in an amount effective to treat the intraocular structure  
20 disorder. In a preferred embodiment, the copolymer includes nominally approximately  
21 50% of each monomer. The copolymer is preferably purified before introduction into  
22 the intraocular structure, for example by removing lower molecular weight impurities in  
23 the copolymer.

24 The copolymer may be introduced into the vitreous, the aqueous, and/or the lens.  
25 The copolymer is particularly well suited as a vitreous replacement retinal tamponade for  
26 vitreoretinal surgery.

27 The copolymer preferably has a viscosity of 175 to 200 cs, a specific gravity of  
28 approximately 1.15, and a refractive index of approximately 1.38. In one use, the  
29 copolymer has dissolved in it before introduction into the intraocular structure an  
30 anti-proliferative agent such as retinoic acid.

31 Also featured is a method of repairing a retinal disorder of an eye comprising  
32 locating the eye so that the choroid is under the retina, and introducing into the vitreous

1 cavity of the eye a liquid copolymer of silicone oil and fluorosilicone oil to maintain the  
 2 retina against the choroid. The retinal disorder may be a detached and/or a torn retina.  
 3 Preferably, the copolymer includes nominally approximately 50% of each monomer, has  
 4 a viscosity of approximately 175 to 200 cs, a specific gravity of approximately 1.15, and  
 5 a refractive index of approximately 1.38. The copolymer is stable and tolerated  
 6 sufficiently so that it may be left in the eye for sufficient time for healing to begin, up  
 7 to eight to ten weeks or longer.

8 Also featured is a method of simultaneously repairing an anterior and posterior  
 9 detached or torn retina comprising replacing at least a portion of the vitreous of the eye  
 10 with a liquid copolymer of silicone oil and fluorosilicone oil to maintain both the anterior  
 11 and posterior retina against the choroid.

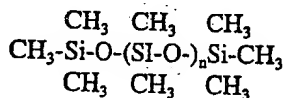
12 This invention also features a method separating adjacent tissue layers comprising  
 13 introducing between the tissue layers a liquid copolymer of silicone oil and fluorosilicone  
 14 oil in an amount sufficient to separate adjacent tissue layers.

#### 16 DISCLOSURE OF PREFERRED EMBODIMENTS

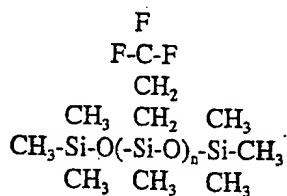
17 Other objects, features and advantages will occur to those skilled in the art from  
 18 the following description of preferred embodiments.

19 This invention may be accomplished in methods of treating eye disorders  
 20 employing a liquid silicone/fluorosilicone copolymer oil.

21 The term "silicone oil" as used herein means polydimethylsiloxane having the  
 22 following formula:

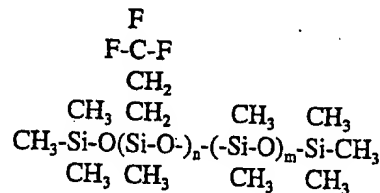


27 The term "fluorosilicone oil" as used herein means polymethyl-3,3,3-  
 28 trifluoropropylsiloxane having the following formula:



The term "perfluorocarbon liquids" as used herein means the compounds disclosed in U.S. Patent No. 4,490,351.

The term "silicone/fluorosilicone copolymer oil", and "copolymer of silicone oil and fluorosilicone oil", as used herein means polymethyl-3,3,3-trifluoropropylsiloxane-dimethylsiloxane copolymer having the following formula:



where n and m may or may not be approximately equal.

The silicone/fluorosilicone copolymer oil used in the methods of this invention is made by copolymerizing the monomers of silicone oil and fluorosilicone oil. The relative amounts of the monomers may be selected to accomplish an oil with the desired properties. The viscosity may be controlled by controlling the polymer chain lengths using methods known in the polymer synthesis field. The result is an oil with the properties listed in Table I as compared to silicone oil and fluorosilicone oil.

Table I

|  | Silicone/<br>Fluorosilicone<br>Copolymer Oil | Silicone Oil | Fluorosilicone Oil |
|--|--|--------------|--------------------|
| Viscosity, cs                              | 5-10,000                                     | 1,000-12,000 | 1,000-10,000       |
| Refractive Index,<br>(@25°C)n <sub>D</sub> | 1.38   | 1.404        | 1.382              |
| Density<br>g/cm <sup>3</sup>               | 1.15   | 0.97         | 1.29               |
| Surface tension,<br>(@37°C) dyne/cm        | 22   | 20           | 23                 |
| Interfacial tension,<br>(@37°C) dyne/cm    | 41   | 44           | 39                 |

Silicone/fluorosilicone copolymer oil thus may be fabricated with a relatively low viscosity of around 800-1000 cs, making it relatively easy to inject and remove from the eye. The viscosity may be adjusted up or down by altering the length of the



1 polymer chains. Viscosities of about 800 cs and greater are believed to assist in  
2 inhibiting emulsification of the oil in the eye. Additionally, silicone/fluorosilicone  
3 copolymer oil has a specific gravity of only 1.15 which allows it to be used to push  
4 back and maintain in place an inferior detached retina without being so dense that it  
5 could damage the retina, thus allowing the copolymer oil to be left in the eye for a  
6 longer time than the perfluorocarbon liquids.

7 The silicone/fluorosilicone copolymer oil also has a relatively high surface and  
8 interfacial tension, making it well suited for manipulation of the retina while  
9 decreasing the likelihood of dispersion and emulsification. Additionally,  
10 silicone/fluorosilicone copolymer oil has only a fraction of the fluorine found in the  
11 fluorosilicone oils and the perfluorocarbon liquids. Accordingly, the  
12 silicone/fluorosilicone copolymer oil does not disperse in the vitreous as readily as  
13 the more fluorinated compounds, the perfluorocarbons.

14 Another advantage of the silicone/fluorosilicone copolymer oil as opposed to the  
15 perfluorocarbon liquids, particularly perfluorophenanthrene, is that the refractive  
16 index is sufficiently different from that of the liquefied vitreous so that the physician  
17 may distinguish between the two in the eye.

18 Crude silicone/fluorosilicone copolymer oil is available from Huls Petrarch  
19 Systems in Bristol, Pennsylvania, as polymethyl-3,3,3-trifluoropropylsiloxane-50%  
20 dimethylsiloxane copolymer. When this crude compound was analyzed by gas  
21 chromatography as previously reported for silicone and fluorosilicone oil in  
22 Inv.Ophthalmol. & Vis. Sci., 31: 2059-2069, 1990, Nakamura K., Refojo, M.F.,  
23 Crabtree, D.V., and Leong, F.L.: Analysis and Fractionation of Silicone and  
24 Fluorosilicone Oils for Intraocular Use, a relatively large amount of low molecular  
25 weight components were detected. There is some speculation that these impurities  
26 are not well tolerated by the tissue of the eye. However, problems associated with  
27 these low molecular weight (under 200 molecular weight) components are generally  
28 unknown and not quantified. Accordingly, the crude, industrial-grade oil may indeed  
29 be of sufficient purity to be used in the eye.

30 If it turns out to be desirable to remove these lower molecular weight  
31 components, there are a number of manners of accomplishing purification, including  
32 chemical extraction, molecular distillation using a wet film still, and filtration. One

1 purification method which is somewhat cumbersome but has worked to effectively  
2 remove the low molecular weight components was by fractionation using the  
3 extraction technique reported in the subject reference. The oil was extracted with  
4 95% ethyl alcohol for six weeks to remove the low molecular weight components.  
5 Then, a rotating evaporator was used to remove the alcohol dissolved in the high  
6 molecular weight fraction of the silicone/fluorosilicone copolymer oil. Any residual  
7 alcohol and low molecular weight components still remaining in the  
8 silicone/fluorosilicone copolymer oil were then removed by distillation under high  
9 vacuum. The silicone/fluorosilicone copolymer oil was then treated with activated  
10 charcoal and filtered twice through filter paper (Whatman No. 114). Finally, the  
11 purified silicone/fluorosilicone copolymer oil was filtered again through a 0.2 micron  
12 filter unit available from Millipore Company. The fractionation procedure yielded  
13 about 60% of the crude silicone/fluorosilicone copolymer oil. No alcoholysis was  
14 observed in the silicone/fluorosilicone copolymer oil. The resulting product was not  
15 soluble in silicone oil or fluorosilicone oil, indicating that it is indeed a different  
16 chemical compound.

17 The methods of this invention are not limited to a silicone/fluorosilicone  
18 copolymer oil having 50% of each monomer. As the proportion of the fluorosilicone  
19 monomer is increased, the specific gravity of the silicone/fluorosilicone copolymer  
20 oil will increase, but the increased number of fluorine atoms will lead to a greater  
21 tendency toward emulsification. In contrast, as the silicone oil monomer portion is  
22 increased above 50%, the specific gravity will decrease and there will be a lesser  
23 tendency to emulsification.

24 The following are several examples of uses of the silicone/fluorosilicone  
25 copolymer oil according to this invention:

26 Example I

27 Because of the high specific gravity and viscous  
28 property of the silicone/fluorosilicone co-polymer, it  
29 can be used as a mechanical tool to flatten and re-attach  
30 large retinal tears of the human eye involving more than  
31 a quadrant of the retina. These tears called Giant Tears  
32 have unfavorable prognosis because their posterior

1 component tends to curl up. The procedure consists of  
2 (1) removal of the vitreous gel by vitrectomy (excision  
3 and removal by means of a vitrector) through the pars  
4 plana of the eye through the microscope, (2) injection  
5 of the co-polymer in the vitreous near the surface of the  
6 retina but posterior to the curled retina, until the  
7 polymer unfurls the retina and fills up the vitreous  
8 cavity, and (3) application of intraocular laser along the  
9 margins of the retinal tear. It takes four to six weeks  
10 for the laser treatment to completely seal and heal the  
11 retinal tear and subsequent removal of the co-polymer  
12 from the eye.  
13

#### 14 Example II

15 By hydraulic forces the co-polymer can be used to  
16 delaminate a sheet of abnormally formed tissue  
17 membrane on the retinal surface by virtue of its weight  
18 and viscosity. This procedure is performed in the  
19 human eye in conjunction with vitrectomy for diabetic  
20 traction retinal membranes and permits the surgeon to  
21 remove retinal tissue membrane safely to flatten retinal  
22 folds. The separated tissue membrane is finally  
23 removed by vitrectomy. The co-polymer is removed  
24 from the eye after the procedure.  
25

#### 26 Example III

27 Another use of the co-polymer is the removal of  
28 accidentally displaced intraocular lens implant or  
29 dislodged lens nuclear fragments in the human eye  
30 during phaco emulsification. Because of the high  
31 specific gravity of the co-polymer, the materials can be  
32 displaced in the front or in the anterior chamber of the

1 eye where they can be repositioned and fixed with a  
2 suture in the case of an intraocular implant, or removal  
3 by phaco emulsification in the case of a nuclear  
4 fragment.

5  
6 Silicone/fluorosilicone copolymer oil is thus useful in the same manner that the  
7 perfluorocarbon liquids, silicone oils and fluorosilicone oils are currently used for.  
8 The intraocular treatments that may be accomplished with silicone/fluorosilicone  
9 copolymer oil include replacement of some or all of the vitreous, typically  
10 accomplished concurrently with removal of the vitreous being replaced. Additionally,  
11 the liquid may be used to replace some or all of the aqueous. The liquid may also  
12 be introduced into the lens to form a substantially transparent window therein.

13 One major use of silicone/fluorosilicone copolymer oil is for vitreoretinal  
14 surgery, particularly as a tamponade for inferior and/or superior detached retinas.  
15 The compound may remain in the eye for at least the eight to ten weeks necessary for  
16 the healing process. Accordingly, detached and/or torn retinas may be repaired with  
17 a single operative procedure as opposed to the two procedures required when using  
18 perfluorocarbon liquids and other substances that may not remain in the eye for a  
19 sufficient time to allow healing to commence. In the procedure, the eye is positioned  
20 so that the choroid is under the retina, and the copolymer is introduced to push the  
21 retina back in place and hold it against the choroid. If the liquid level covers the  
22 detachment, the weight of the liquid will gently maintain the retina in place against  
23 the choroid until healing at least commences.

24 Silicone/fluorosilicone copolymer oil may also be used for other procedures  
25 accomplished with inert liquids. For example, hydraulic laminar separation or  
26 hydrodissection to separate tissue layers may be accomplished by injecting  
27 silicone/fluorosilicone copolymer oil between the tissue layers in an amount sufficient  
28 to separate the layers.

29 There are a number of drugs which are used to treat disorders of the eye. The  
30 silicone/fluorosilicone copolymer oil of this invention may be used as a vehicle to  
31 deliver those drugs directly to the areas requiring treatment, which should be more  
32 effective than the currently used intravenous delivery techniques. The oil could be

1 used to deliver any drug which could be delivered along with the oil through the  
2 needle used for delivery, including liquid, powdered, and drug microspheres. This  
3 invention is meant to encompass the delivery of any drug along with the copolymer  
4 oil.

5 Examples of known drugs which can be delivered are as follows:

6 Anti-proliferative drugs such as the vitamin A derivative retinoic acid are used  
7 to prevent unwanted growth in the posterior chamber of the eye, as a treatment for  
8 proliferative retinopathy (PVR). However, retinoic acid is not liposoluble, and only  
9 liposoluble drugs can be dissolved in silicone oils. No drug will dissolve in the  
10 perfluorocarbon liquids. It has been found that retinol and retinoic acid dissolve in  
11 silicone/fluorosilicone copolymer oil, thus creating the possibility of delivering an  
12 anti-proliferative agent into the vitreous cavity along with the silicone/fluorosilicone  
13 copolymer oil, which can thus be used not only as the tamponade agent, but also as  
14 the vehicle for the delivery of the drug.

15 There are also drugs which are used to treat CMV retinitis, including Foscarnet,  
16 made by Astra Pharmaceutical, Westboro, Massachusetts, and Gancyclovir, made by  
17 Syntex, Palo Alto, California. These drugs temporarily halt the progression of the  
18 disease, and are currently administered intravenously. The copolymer oil of this  
19 invention may be used as a vehicle for delivering these drugs directly to the posterior  
20 chamber of the eye so that they can act on the retina.

21 Although specific features of the invention are shown in some drawings and not  
22 others, this is for convenience only as some feature may be combined with any or all  
23 of the other features in accordance with the invention.

24 Other embodiments will occur to those skilled in the art and are within the  
25 following claims:

26 What is claimed is:

CLAIMS

1. A method of manipulating the retina, holding the retina in place, displacing a disclosed lens, or delaminating tissue in the eye, comprising introducing into the eye a liquid silicone/fluorosilicone copolymer oil in an amount effective to accomplish the method.
2. The method of claim 1 in which said copolymer includes nominally approximately 50% of each monomer.
3. The method of claim 1 in which said copolymer is purified before introduction into the intraocular structure.
4. The method of claim 3 in which the purification removes lower molecular weight impurities in the copolymer.
5. The method of claim 1 in which said copolymer is introduced into the vitreous of the eye.
6. The method of claim 1 in which said copolymer is introduced into the aqueous of the eye.
7. The method of claim 1 in which said copolymer has introduced into it, before introduction into the intraocular structure, an anti-proliferative agent.
8. The method of claim 7 in which said anti-proliferative agent includes retinoic acid or retinol.
9. The method of claim 1 in which said copolymer has a viscosity of approximately 175-200 cs.
10. The method of claim 1 in which said copolymer has a specific gravity of approximately 1.15.

11. The method of claim 1 in which said copolymer has a refractive index of approximately 1.38.

12. The method of claim 1 in which said copolymer is introduced into the lens of the eye.

13. The method of claim 1 further including the step of adding a drug or other substance to the liquid silicone/fluorosilicone copolymer oil before its introduction into the eye.

14. A method of manipulating a detached or torn retina comprising locating the eye so that the choroid is under the retina, and introducing into the vitreous cavity of the eye a liquid silicone/fluorosilicone copolymer oil in amount sufficient to maintain the retina against the choroid.

15. The method of claim 14 in which said copolymer includes nominally approximately 50% of each monomer.

16. The method of claim 14 in which said copolymer has a viscosity of approximately 175-200 cs.

17. The method of claim 14 in which said copolymer has a specific gravity of approximately 1.15.

18. The method of claim 14 in which said copolymer has a refractive index of approximately 1.38.

19. The method of claim 14 in which said copolymer is left in the eye for sufficient time for healing to begin.

20. A method of simultaneously repairing an anterior and posterior detached or torn retina comprising replacing at least a portion of the vitreous of the eye with a liquid silicone/fluorosilicone copolymer oil in an amount sufficient to maintain the anterior and posterior retina against the choroid.

1           21. A method of separating adjacent tissue layers comprising introducing  
2           between said tissue layers a liquid silicone/fluorosilicone copolymer oil in an amount  
3           sufficient to separate said adjacent tissue layers.  
4

5           22. A method of manipulating the retina, holding the retina in place,  
6           displacing a dislocated lens, delaminating tissue in the eye, or delivering a drug into  
7           the eye, comprising introducing into the eye a liquid silicone/fluorosilicone copolymer  
8           oil in an amount effective to accomplish the method.  
9

10          23. The method of claim 22 in which said copolymer includes nominally  
11          approximately 50% of each monomer.  
12

13          24. The method of claim 22 in which said copolymer is introduced into the  
14          vitreous of the eye.  
15

16          25. The method of claim 22 in which said copolymer is introduced into the  
17          aqueous of the eye.  
18

19          26. The method of claim 22 in which said copolymer is introduced into the  
20          lens of the eye.  
21

22          27. The method of claim 22 in which said copolymer has a drug dissolved  
23          in it before introduction into the eye.  
24

25          28. The method of claim 27 in which the drug includes an anti-proliferative  
26          agent.  
27

28          29. The method of claim 28 in which the anti-proliferative agent is retinoic  
29          acid or retinol.  
30

31          30. The method of claim 22 in which said copolymer has a viscosity of  
32          approximately 5-10,000 cs.  
33  
34



1           31. The method of claim 22 in which said copolymer has a specific gravity  
2 of approximately 1.15.

3  
4           32. The method of claim 22 in which said copolymer has a refractive index  
5 of approximately 1.38.

6  
7           33. The method of claim 22 in which a detached or torn retina is  
8 manipulated by locating the eye so that the choroid is under the retina, and  
9 introducing into the vitreous cavity of the eye a liquid silicone/fluorosilicone  
10 copolymer oil in an amount sufficient to maintain the retina against the choroid.

11  
12           34. The method of claim 33 in which said copolymer is left in the eye for  
13 sufficient time for healing to begin.

# INTERNATIONAL SEARCH REPORT

in national application No.  
PCT/US94/02383

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(5) : A61K 31/74

US CL : 424/78.04; 514/912.

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/78.04; 514/912

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|-----------|--|-----------------------|
| A         | US, A, 4,490,351 (CLARK, JR.) 25 DECEMBER 1984, ENTIRE DOCUMENT.                   | 1-34                  |

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

|     |   |     |  |
|-----|---|-----|--|
| *A* | document defining the general state of the art which is not considered to be part of particular relevance   | *T* | later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention  |
| *B* | earlier document published on or after the international filing date  | *X* | document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone   |
| *L* | document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) | *Y* | document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art |
| *O* | document referring to an oral disclosure, use, exhibition or other means  | *Z* | document member of the same patent family  |
| *P* | document published prior to the international filing date but later than the priority date claimed  |     |  |

Date of the actual completion of the international search

25 MAY 1994

Date of mailing of the international search report

02 JUN 1994

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